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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/744,247	01/30/2001	Francesco Parenti	199509US0PCT	4708

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EXAMINER	
LUKTON, DAVID	
ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 11/14/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/744,247	PARENTI ET AL.	
	Examiner	Art Unit	
	David Lukton	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 August 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-42* is/are pending in the application.

4a) Of the above claim(s) *19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18 and 20-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Applicants' species election is acknowledged (ramoplanin A2). Pursuant to the directives of paper No. 9 (filed 8/30/02), claims 7 and 14 have been amended, and claims 36-42 added. Claims 1-42 are pending. Claims 6 and 8 are now rejoined with the elected Group. Claims 1-17, 20-42 are examined in this Office action; claim 18 is examined in part. Claim 19 remains withdrawn from consideration.

*

An abstract is required, and does not appear to be present.

*

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 14 is drawn to a method for treating infections that are caused by "microorganisms". Applicants have demonstrated some efficacy in the treatment of infections cause by *Ent. faecium, Staph. aureus*, and *Strep. pneumonia.* There are two issues here. First, it is asserted in claim 14 that bacterial infections can be successfully treated if the bacterial species is susceptible to the effects of an "antibiotic of the ramoplanin family". The phrase "antibiotic of the ramoplanin family", however, is not limited to compounds of formula I (claim 1). Assuming that it is possible to

determine exactly what might be encompassed by "antibiotics of the ramoplanin family", it would certainly include compounds other than those of formula I. Thus, as a first step, one would have to determine the efficacy of all such antibiotics. Next, one would have to test each of the compounds of formula I and each of the "fat emulsion products" to determine which is equal in efficacy to those compounds which are "antibiotics of the ramoplanin family", but are not, at the same time, formulations occurring within the scope of claim 1. "Undue experimentation" would be required for this. It is suggested that the antibiotics in question are those that are encompassed by formula I.

Second, there is the matter of what is encompassed by the term "microorganism". This term encompasses viruses and certain parasites, in addition to bacteria. As it happens, few compounds, if any, are effective at treating infections caused by bacteria, and at the same time, effective also against infections caused by either viruses or parasites. The reality is that most compounds which show promise *in vitro* in the treatment of viruses or parasites are not effective when administered to an infected mammal. For applicants convenience, the following is a listing of that references discuss the matter of parasitic infections in animals and humans:

Urbani C (*Tropical Medicine and International Health* 6 (11) 935-44, 2001)

Geerts S (*Clinical Microbiology Reviews* 13 (2) 207-22, 2000)

Larsen, M (*International Journal for Parasitology* 29 (1) 139-46, 1999)

Stephenson (*Drugs* 60 (5) 985-95, 2000);

Cutrona (*Comprehensive Therapy*, 20 (8) 445-58, 1994)

Mandell (*Medical Clinics of North America* 72 (3) 669-90, 1988).

Roos M. H. (*Pharmacology and Therapeutics* **60** (2) 331-6, 1993

Borst P. (*Annual Review of Microbiology* **49**, 427-60, 1995)

Tarleton (*International Journal for Parasitology* **31**(5-6) 550-554, 2001)

Docampo (*Current Pharmaceutical Design* **7**(12) 1157-64, 2001)

Parasitic infections include malaria, trypanosomiasis, schistosomiasis, onchocerciasis, leishmaniasis, amebiasis, ascariasis, babesiosis, balantidiasis, enterobius, fiarisis, blood flukes, giaridasis, hookworm, strongyloidiasis, tapeworm, toxoplasmosis, trichinosis, and trichuriasis.

As indicated above, most compounds which show promise *in vitro* in the treatment of viruses or parasites are not effective when administered to an infected mammal. But when a skilled microbiologist has not even attempted to determined whether a given compound is effective to inhibit virus or parasite propagation in a petri dish, the probability of efficacy in vivo becomes vanishingly small. Such is the present situation. "Undue experimentation" would be required to treat parasitic or viral infections using the claimed formulations. It is suggested that claim 14 be limited to

treatment of infections caused by bacteria.

*

Claims 1-18, 20-42 are rejected under 35 U.S.C. §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- Claim 1 should begin with the indefinite article (**A** pharmaceutical formulation).

- Claim 1 recites (third line from last) the phrase "fat emulsion product". How is a "fat emulsion" different from a "fat emulsion product"....? A related matter concerns the phrase "the oil phase" (last line of the claim). This phrase lacks antecedent basis. In response, applicants have argued that the examiner is "confused" by the term at issue. However, the level of insight of the examiner into applicants' intentions is not the factor that determines the degree of definiteness or indefiniteness. Rather, the degree of indefiniteness is determined by a reading of the claim. Applicants have argued that if one were to read the specification begining on page 5, line 25, they would be able to ascertain the dividing line between (a) those compositions which contain both lipids and water yet are not fat emulsion products, and (b) those compositions which contain both lipids and water and which <u>are</u> fat emulsion products. Certainly this would not be true for the drug formulation specialist who was not in possession of the various cited references ("the Extra Pharmacopia", "Vidal", and "Submicron Emulsions..."). Exactly what the skilled drug formulation specialist might ascertain after a reading of the cited references cannot be determined at this time. It is suggested that applicants "extract out" whatever information from the specification is deemed appropriate, and incorporate this into the claim language.

- In claim 6, the weight percentages do not add up to 100%, thus rendering the claim indefinite.

- In claim 7 the term "quite small" is used. Where is the dividing line between, e.g., "quite small", very small, and somewhat small?

- In claim 7, the quantities listed for soybean oil, safflower oil, posphoplipid and glycerol 13.45% in the case of "fat emulsion product 1". What is the remaining 86.55%...?

- Claim 1 is indefinite as to the upper limit of "the oil phase". Can "the oil phase" constitute 100% of the "fat emulsion product"...?

- Claim 14 makes reference to "antibiotics of the ramoplanin family". The wording of the claim is such as to go beyond the compounds of formula I. What other compounds are intended?

- Claim 15 recites that term "infections" in the plural; claim 42, on the other hand recites "infection" in the singular. Given the dependence of claim 42 on claim 15, there is a mismatch between the singular of claim 42 and the plural of claim 15. A related issue concerns claim 42. Claim 42 encompasses the possibility of a patient having two or three different infections simultaneously. Yet the claim is drawn to the treatment of just one infection. Accordingly, there is a subtle contradiction.

*

The following is a quotation of 35 USC §103 which forms the basis for all obviousness rejections set forth in the Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made, absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention

dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

Claims 1-2 are rejected under 35 U.S.C. §103 as being unpatentable over Assi (EP 0,318,680) in view of (a) Kurihara (USP 4,990,337) or (b) Sekine (USP 5,968,899) or (c) Ishida (USP 5,891,846).

Assi discloses the structure of ramoplanin which falls within the scope of that recited in instant claim 1. The reference does not specifically suggest an emulsion. Each of the secondary references teaches the use of an emulsion to enhance bioavailability. None of the secondary references mentions ramoplanin. Thus, it would have been obvious to one of ordinary skill to formulate ramoplanin into an emulsion. The phrase "for intravenous administration" (instant claim 1) is noted, but this intended use phrase does not necessarily distinguish formulations intended for other routes of administration. Moreover, the term "fat emulsion product" is sufficiently vague as to encompass compositions that are also useful for oral administration.

Thus, the claim is rendered obvious.

*

Claims 1-2 are rejected under 35 U.S.C. §103 as being unpatentable over Romeo, B. (*Program and Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy*, (1993) Vol. 33, No. 0, pp. 200. Meeting Info.: 33rd Interscience Conference on Antimicrobial Agents and Chemotherapy New Orleans, Louisiana, USA

October 17-20, 1993) in view of Owen (USP 5,688,761).

Romeo discloses that oral bioavailabiltiy of ramoplanin is low. Romeo does not disclose emulsions. Owen discloses emulsions for administering peptides. As disclosed at col 9, line 15, the emuslions are useful for administering drugs that exhibit low oral bioavailability. Also disclosed (col 7, lines 4-5; col 20, line 1+) is i.v. administration.

Thus, it would have been obvious to one of ordinary skill to employ the emulsions of Owen in order to attain increased bioavailability.

*

Claims 1-2 are rejected under 35 U.S.C. §103 as being unpatentable over Romeo, B (*Microbial Ecology in Health and Disease*, (1992) Vol. 2, No. 6, pp. XX. Meeting Info.: XVII International Congress on Microbial Ecology and Disease Helsinki, Finland August 28-29, 1992) in view of Owen (USP 5,688,761).

Romeo discloses that oral bioavailabiltiy of ramoplanin is low. Romeo does not disclose emulsions. Owen discloses emulsions for administering peptides. As disclosed at col 9, line 15, the emuslions are useful for administering drugs that exhibit low oral bioavailability. Also disclosed (col 7, lines 4-5; col 20, line 1+) is i.v. administration.

Thus, it would have been obvious to one of ordinary skill to employ the emulsions of

Owen in order to attain increased bioavailability.

*

Claims 1-2 are rejected under 35 U.S.C. §103 as being unpatentable over Posanski (US 2002/0099067).

Posanski discloses emulsions that contain any of several therapeutic agents. One of those (paragraph 17, 11th line from last) is ramoplanin. Posanski does not "single out" ramoplanin, however one of ordinary skill would recognized that this possibility is encompassed.

Thus, the claims are rendered obvious.

*

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 703-308-3213. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached at (703) 308-2923. The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

DAVID LUKTON
PATENT EXAMINER
GROUP 1600